to robotic methods for combinatorial library synthesis and testing, minimizes the storage requirements for combinatorial libraries, and allows for simpler and faster compound identification.

L8   ANSWER 3 OF 4   CAPLUS   COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:2523   CAPLUS
DOCUMENT NUMBER: 137:93369
TITLE: A one-bead, one-stock solution approach to chemical
                         genetics: part 2
AUTHOR(S):   Clemons, Paul A.; Koehler, Angela N.; Wagner, Bridget
                         K.; Sprigings, Timothy G.; Spring, David R.; King,
                         Randall W.; Schreiber, Stuart L.; Foley, Michael A.
CORPORATE SOURCE: Howard Hughes Medical Institute at Harvard University,
                         Cambridge, MA, 02138, USA
SOURCE: Chemistry & Biology (2001), 8(12), 1183-1195
                         CODEN: CBOLE2; ISSN: 1074-5521
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
IT   438625-00-4P 438625-04-8P
     RL: CPN (Combinatorial preparation); PAC (Pharmacological activity); BIOL
     (Biological study); CMBI (Combinatorial study); PREP (Preparation)
         (bead arraying, processing, and assaying in one-bead, one-stock solution
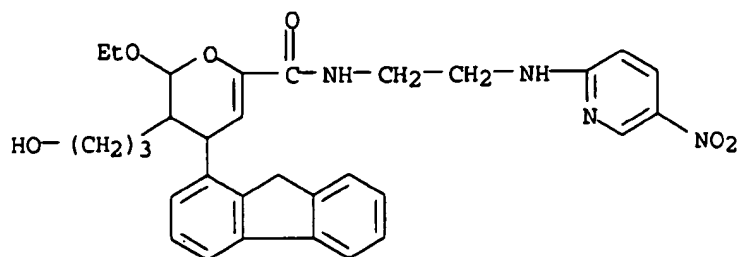   approach to chemical genetics)
RN   438625-00-4   CAPLUS
CN   2H-Pyran-6-carboxamide, 2-ethoxy-4-(9H-fluoren-1-yl)-3,4-dihydro-3-[2-[2-
     (2-hydroxyethoxy)ethoxy]ethyl]-N-[2-(5-methoxy-1H-indol-3-yl)ethyl]- (9CI)
     (CA INDEX NAME)
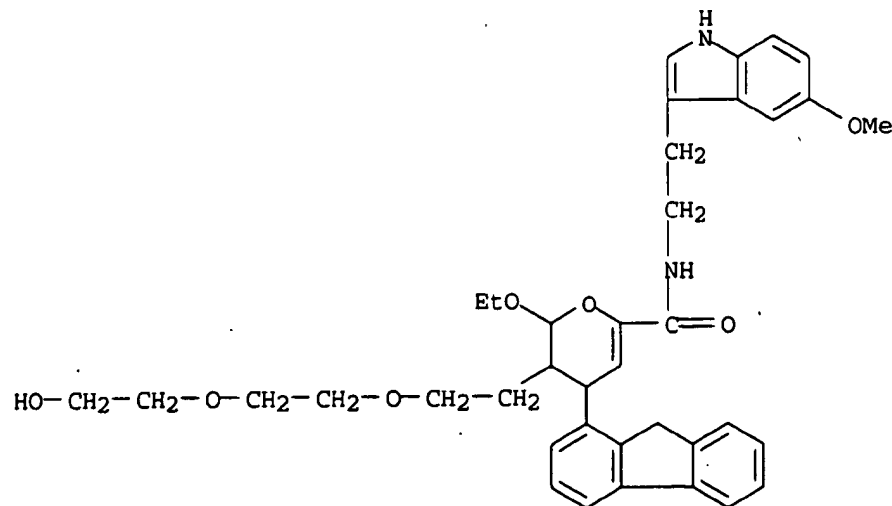
RN   438625-04-8   CAPLUS
CN   2H-Pyran-6-carboxamide, 2-ethoxy-4-(9H-fluoren-1-yl)-3,4-dihydro-3-(3-
     hydroxypropyl)-N-[2-[(5-nitro-2-pyridinyl)amino]ethyl]- (9CI)   (CA INDEX
     NAME)

EtO— ... C—NH—CH2—CH2—NH— ... NO2

HO—(CH2)3

AB   Background: Chemical genetics provides a systematic means to study biol.
      using small mols. to effect spatial and temporal control over protein
      function. As complementary approaches, phenotypic and proteomic screens
      of structurally diverse and complex small mols. may yield not only
      interesting individual probes of biol. function, but also global
      information about small mol. collections and the interactions of their
      members with biol. systems. Results: We report a general high-throughput
      method for converting high-capacity beads into arrayed stock solns.
      amenable to both phenotypic and proteomic assays. Polystyrene beads from
      diversity-oriented syntheses were arrayed individually into wells. Bound
      compds. were cleaved, eluted, and resuspended to generate 'mother plates'
      of stock solns. The second phase of development of our technol. platform
      includes optimized cleavage and elution conditions, a novel bead arraying
      method, and robotic distribution of stock solns. of small mols. into
      'daughter plates' for direct use in chemical genetic assays. This library
      formatting strategy enables what we refer to as annotation screening, in
      which every member of a library is annotated with biol. assay data. This
      phase was validated by arraying and screening 708 members of an encoded
      4320-member library of structurally diverse and complex
      dihydropyrancarboxamides. Conclusions: Our 'one-bead, multiple-stock
      solution' library formatting strategy is a central element of a technol.
      platform aimed at advancing chemical genetics. Annotation screening provides
      a means for biol. to inform chemical, complementary to the way that chemical
can
      inform biol. in conventional ('investigator-initiated') small mol.
      screens.

REFERENCE COUNT: 28   THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS
                                   RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

prepared A library of 4320 dihydropyrancarboxamides was prepared; claimed
title compound (II) was shown to be inhibitory against Eg5 kinesin. Solid
support synthesis and decoding methodolgy is described.

L8   ANSWER 2 OF 4   CAPLUS   COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:112577 CAPLUS
DOCUMENT NUMBER: 136:150765
TITLE: Decoding products of diversity pathways from stock
                         solutions derived from single polymeric macrobeads
AUTHOR(S):   Blackwell, Helen E.; Perez, Lucy; Schreiber, Stuart L.
CORPORATE SOURCE: Howard Hughes Medical Institute, Harvard Institute of
                         Chemistry and Cell Biology, Harvard University,
                         Cambridge, MA, 02138, USA
SOURCE: Angewandte Chemie, International Edition (2001),
                         40(18), 3421-3425
                         CODEN: ACIEF5; ISSN: 1433-7851
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
IT   394252-96-1P 394253-07-7P 394253-10-2P
      394253-11-3P 394253-12-4P 394253-25-9P
      394253-26-0P 394253-35-1P 394253-42-0P
      394253-49-7P 394253-50-0P 394253-58-8P
      394253-60-2P 394253-61-3P 394253-64-6P
      394253-68-0P 394253-76-0P 395072-36-3P
   395072-37-4P
      RL: CPN (Combinatorial preparation); CMBI (Combinatorial study); PREP
      (Preparation)
          (chloroarom. diazoketone tags and stock solns. in preparation and decoding
          and deconvolution of combinatorial libraries on macrobeads and use in
          preparation of nonracemic dihydropyrancarboxamide combinatorial library)
RN   394252-96-1 CAPLUS
CN   2H-Pyran-6-carboxamide, 4-(1,3-benzodioxol-5-yl)-2-ethoxy-3,4-dihydro-3-[2-
      [2-(2-hydroxyethoxy)ethoxy]ethyl]-N-[2-(5-methoxy-1H-indol-3-yl)ethyl]-,
      (2R,3R,4S)- (9CI)   (CA INDEX NAME)
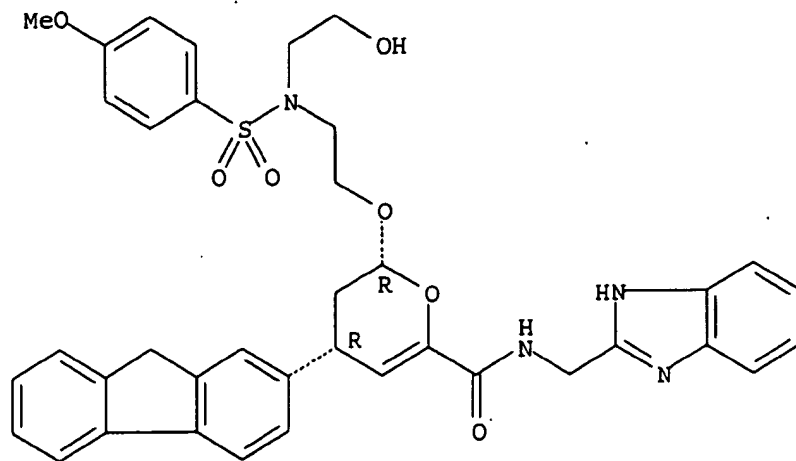
Absolute stereochemistry.
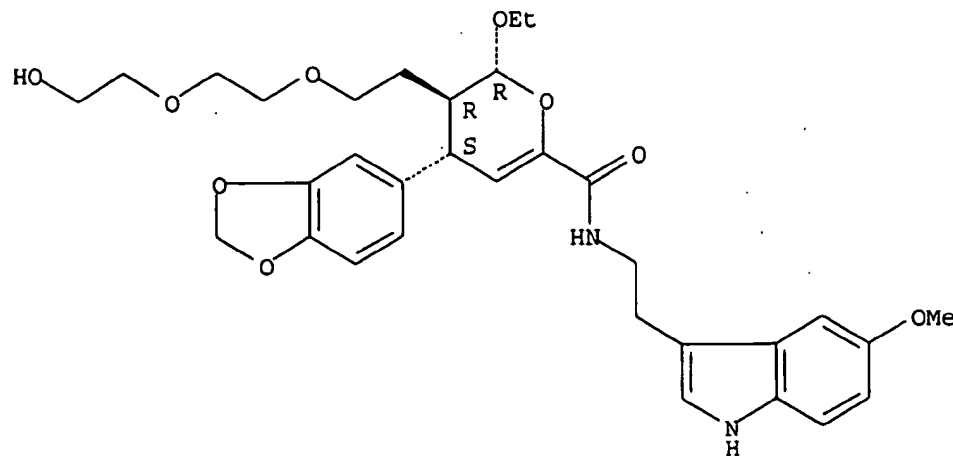
RN   394253-07-7 CAPLUS
CN   2H-Pyran-6-carboxamide, N-(1H-benzimidazol-2-ylmethyl)-4-(9H-fluoren-2-yl)-
      3,4-dihydro-2-[2-[(2-hydroxyethyl)[(4-methoxyphenyl)sulfonyl]amino]ethoxy]-

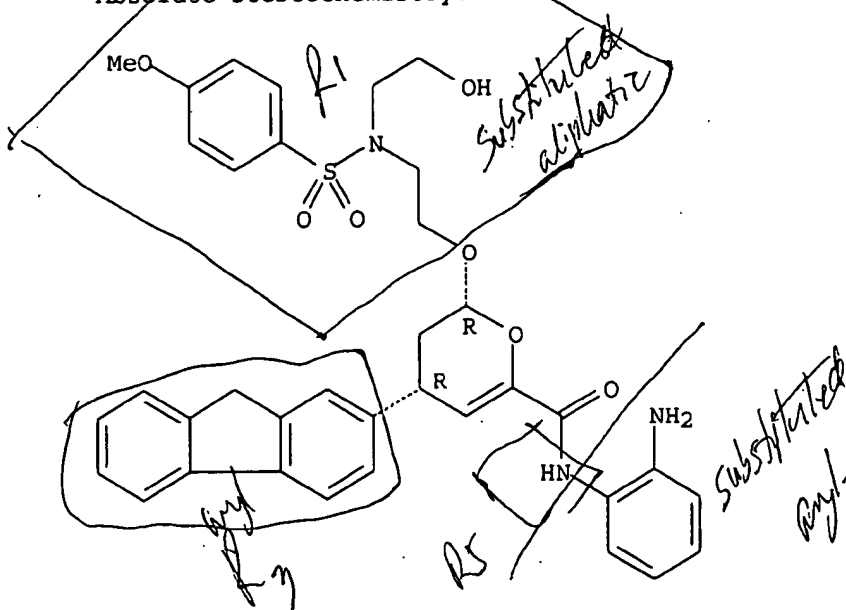, (2R,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN   394253-10-2 CAPLUS
CN   2H-Pyran-6-carboxamide, N-(2-aminophenyl)-4-(9H-fluoren-2-yl)-3,4-dihydro-
     2-[2-[(2-hydroxyethyl)[(4-methoxyphenyl)sulfonyl]amino]ethoxy]-, (2R,4R)-
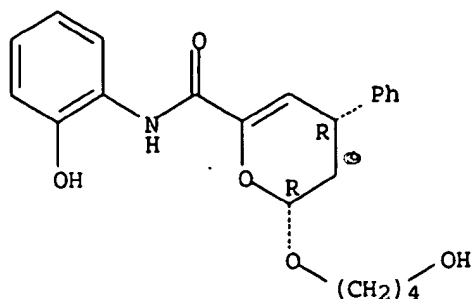   (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN   394253-11-3 CAPLUS
CN   2H-Pyran-6-carboxamide, 3,4-dihydro-2-(4-hydroxybutoxy)-N-(2-
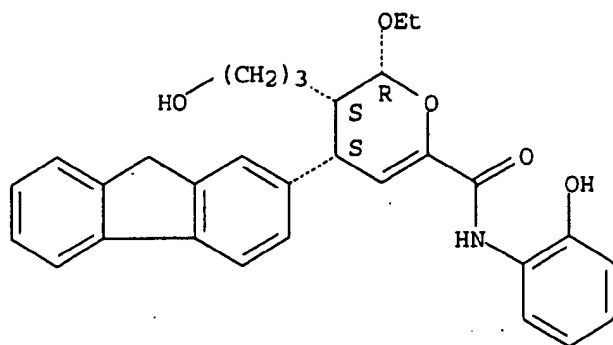   hydroxyphenyl)-4-phenyl-, (2R,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 394253-12-4 CAPLUS
CN 2H-Pyran-6-carboxamide, 2-ethoxy-4-(9H-fluoren-2-yl)-3,4-dihydro-N-(2-hydroxyphenyl)-3-(3-hydroxypropyl)-, (2R,3S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 394253-25-9 CAPLUS
CN 2H-Pyran-6-carboxamide, 2-ethoxy-4-(9H-fluoren-2-yl)-3,4-dihydro-3-(3-hydroxypropyl)-N-[2-[(5-nitro-2-pyridinyl)amino]ethyl]-, (2R,3S,4S)- (9CI) (CA INDEX NAME)
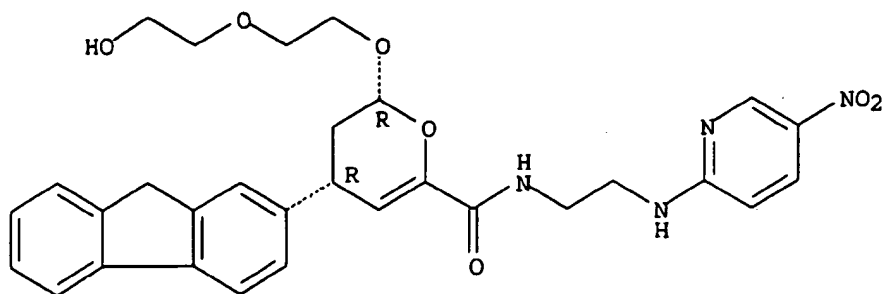
Absolute stereochemistry.
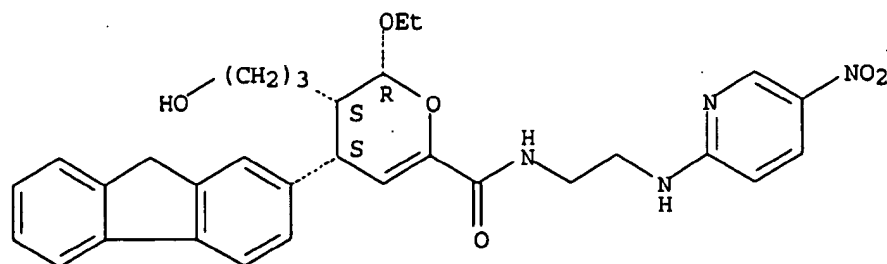
RN 394253-26-0 CAPLUS
CN 2H-Pyran-6-carboxamide, 4-(9H-fluoren-2-yl)-3,4-dihydro-2-[2-(2-hydroxyethoxy)ethoxy]-N-[2-[(5-nitro-2-pyridinyl)amino]ethyl]-, (2R,4R)- (9CI) (CA INDEX NAME)
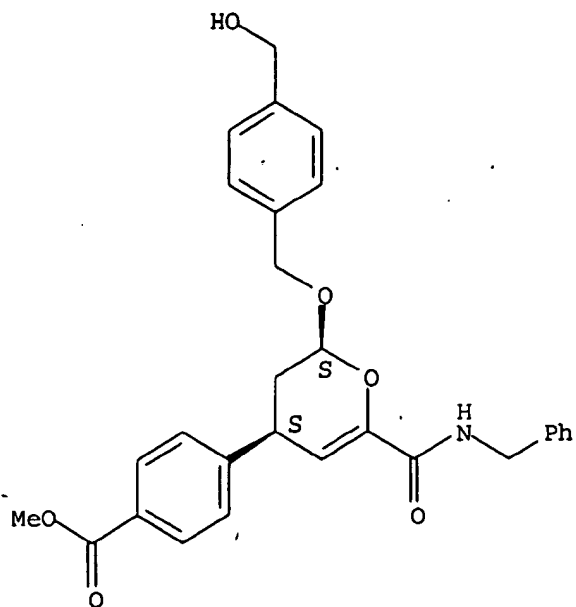
Absolute stereochemistry.

RN   394253-35-1 CAPLUS
CN   Benzoic acid, 4-[(2S,4S)-3,4-dihydro-2-[[4-(hydroxymethyl)phenyl]methoxy]-
      6-[[(phenylmethyl)amino]carbonyl]-2H-pyran-4-yl]-, methyl ester (9CI) (CA
      INDEX NAME)

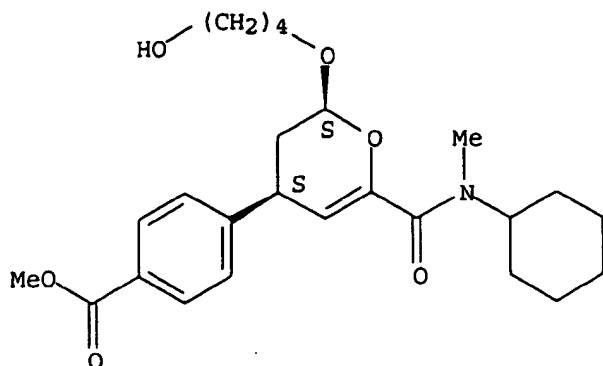Absolute stereochemistry.

RN   394253-42-0 CAPLUS
CN   Benzoic acid, 4-[(2S,4S)-6-[(cyclohexylmethylamino)carbonyl]-3,4-dihydro-2-
      (4-hydroxybutoxy)-2H-pyran-4-yl]-, methyl ester (9CI) (CA INDEX NAME)
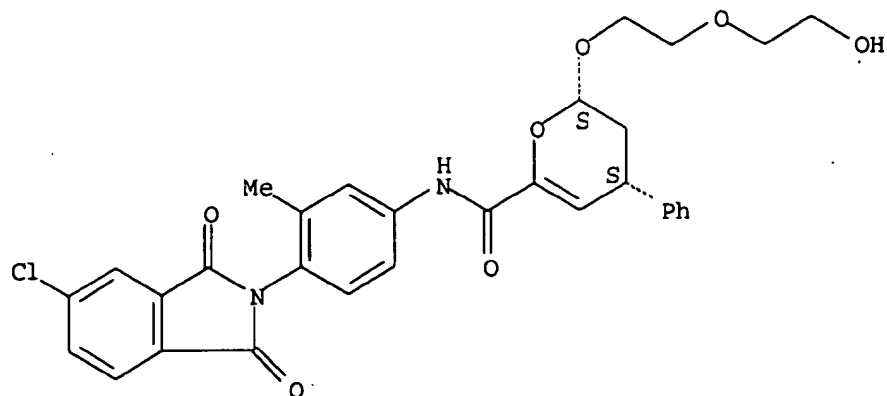
Absolute stereochemistry.

RN 394253-49-7 CAPLUS
CN 2H-Pyran-6-carboxamide, N-[4-(5-chloro-1,3-dihydro-1,3-dioxo-2H-isoindol-2-
yl)-3-methylphenyl]-3,4-dihydro-2-[2-(2-hydroxyethoxy)ethoxy]-4-phenyl-,
(2S,4S)- (9CI) (CA INDEX NAME)
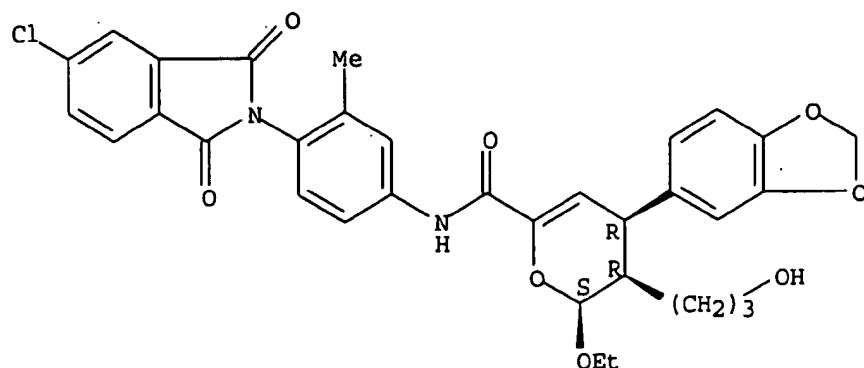
Absolute stereochemistry.

RN 394253-50-0 CAPLUS
CN 2H-Pyran-6-carboxamide, 4-(1,3-benzodioxol-5-yl)-N-[4-(5-chloro-1,3-
dihydro-1,3-dioxo-2H-isoindol-2-yl)-3-methylphenyl]-2-ethoxy-3,4-dihydro-3-
(3-hydroxypropyl)-, (2S,3R,4R)- (9CI) (CA INDEX NAME)
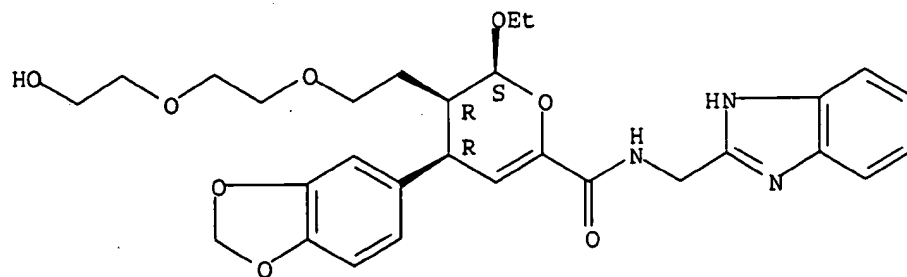
Absolute stereochemistry.

RN   394253-58-8   CAPLUS
CN   2H-Pyran-6-carboxamide, N-(1H-benzimidazol-2-ylmethyl)-4-(1,3-benzodioxol-
     5-yl)-2-ethoxy-3,4-dihydro-3-[2-[2-(2-hydroxyethoxy)ethoxy]ethyl]-,
     (2S,3R,4R)- (9CI)   (CA INDEX NAME)

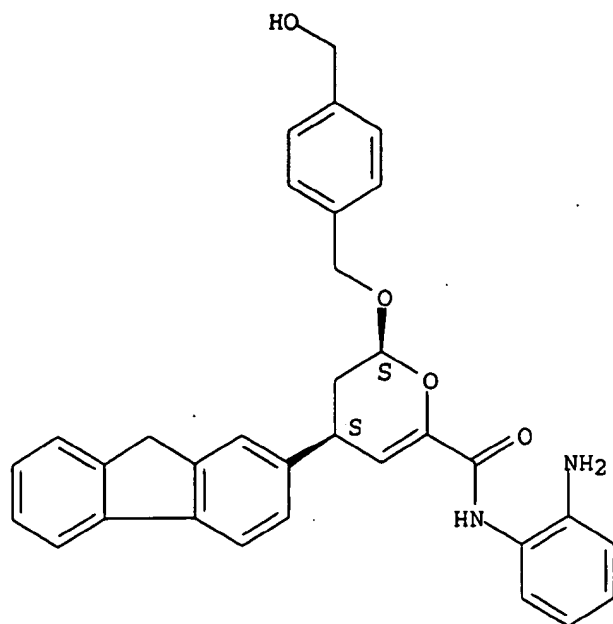Absolute stereochemistry.

RN   394253-60-2   CAPLUS
CN   2H-Pyran-6-carboxamide, N-(2-aminophenyl)-4-(9H-fluoren-2-yl)-3,4-dihydro-
     2-[[4-(hydroxymethyl)phenyl]methoxy]-, (2S,4S)- (9CI)   (CA INDEX NAME)
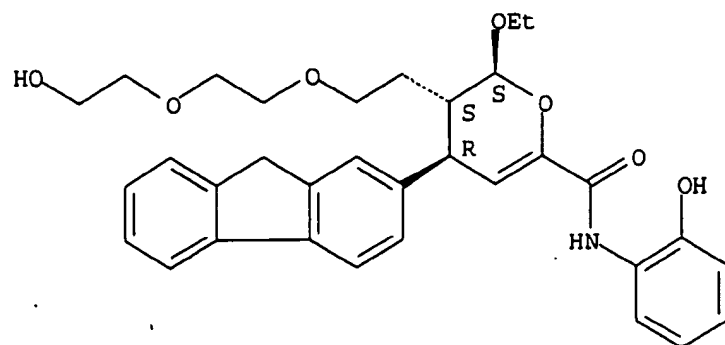
Absolute stereochemistry.

RN 394253-61-3 CAPLUS
CN 2H-Pyran-6-carboxamide, 2-ethoxy-4-(9H-fluoren-2-yl)-3,4-dihydro-3-[2-[2-(2-hydroxyethoxy)ethoxy]ethyl]-N-(2-hydroxyphenyl)-, (2S,3S,4R)- (9CI) (CA INDEX NAME)
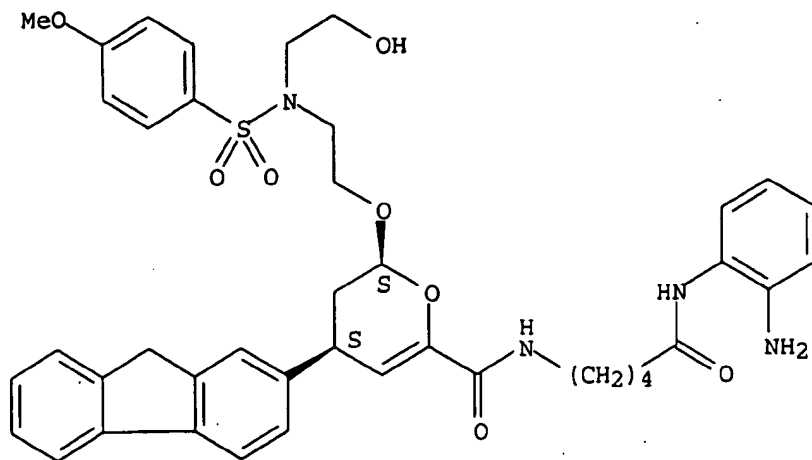
Absolute stereochemistry.

RN 394253-64-6 CAPLUS
CN 2H-Pyran-6-carboxamide, N-[5-[(2-aminophenyl)amino]-5-oxopentyl]-4-(9H-fluoren-2-yl)-3,4-dihydro-2-[2-[(2-hydroxyethyl)[(4-methoxyphenyl)sulfonyl]amino]ethoxy]-, (2S,4S)- (9CI) (CA INDEX NAME)
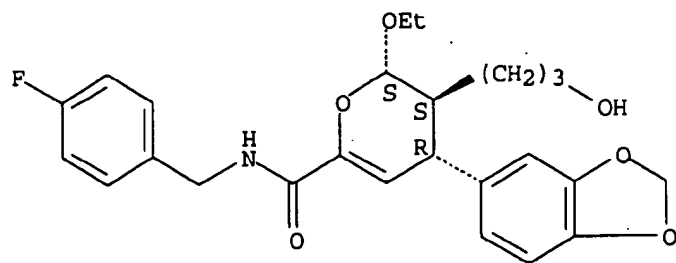
Absolute stereochemistry.

RN   394253-68-0   CAPLUS
CN   2H-Pyran-6-carboxamide, 4-(1,3-benzodioxol-5-yl)-2-ethoxy-N-[(4-
      fluorophenyl)methyl]-3,4-dihydro-3-(3-hydroxypropyl)-, (2S,3S,4R)- (9CI)
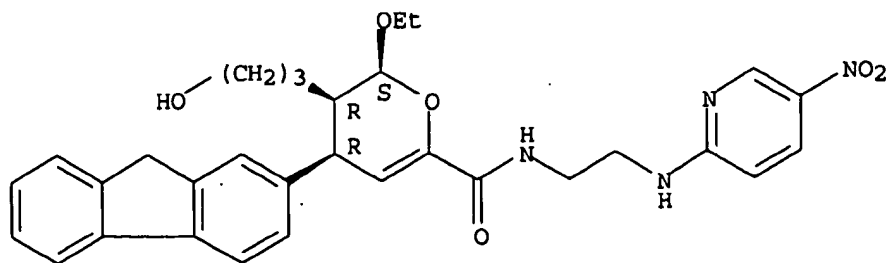   (CA INDEX NAME)

Absolute stereochemistry.

RN   394253-76-0   CAPLUS
CN   2H-Pyran-6-carboxamide, 2-ethoxy-4-(9H-fluoren-2-yl)-3,4-dihydro-3-(3-
      hydroxypropyl)-N-[2-[(5-nitro-2-pyridinyl)amino]ethyl]-, (2S,3R,4R)- (9CI)
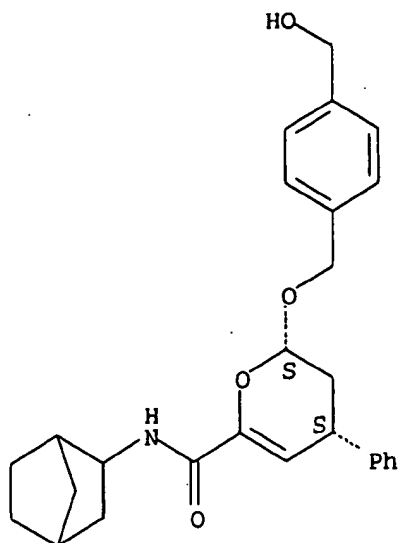   (CA INDEX NAME)

Absolute stereochemistry.

RN   395072-36-3   CAPLUS
CN   2H-Pyran-6-carboxamide, N-bicyclo[2.2.1]hept-2-yl-3,4-dihydro-2-[(4-

(hydroxymethyl)phenyl]methoxy]-4-phenyl-, (2S,4S)- (9CI)   (CA INDEX NAME)
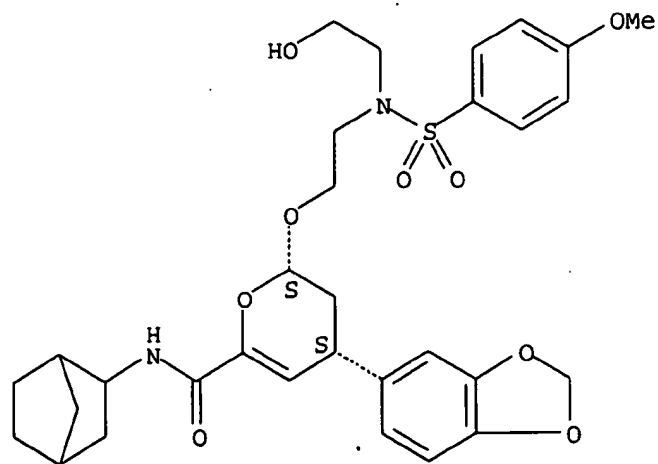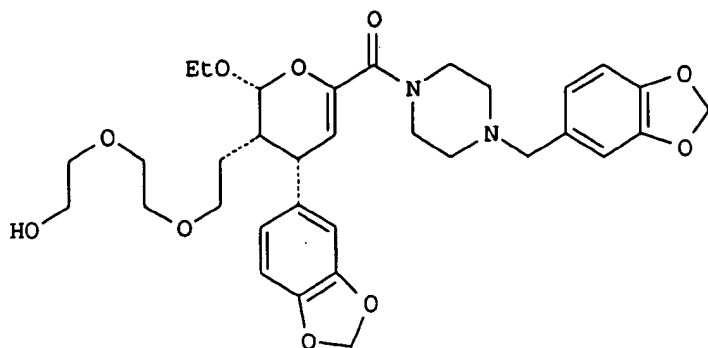
Absolute stereochemistry.

RN   395072-37-4   CAPLUS
CN   2H-Pyran-6-carboxamide, 4-(1,3-benzodioxol-5-yl)-N-bicyclo[2.2.1]hept-2-yl-
      3,4-dihydro-2-[2-[(2-hydroxyethyl)[(4-methoxyphenyl)sulfonyl]amino]ethoxy]-
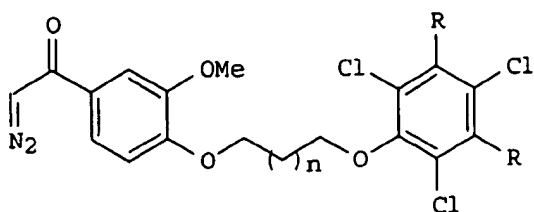   , (2S,4S)- (9CI)   (CA INDEX NAME)

Absolute stereochemistry.

GI

I

II

AB A combinatorial library of nonracemic dihydropyrancarboxamides such as I [prepared on solid phase by the enantioselective Diels-Alder cycloaddn. of resin-bound vinyl ethers with allyl β,γ-unsatd.-α-
ketoesters in the presence of nonracemic bisoxazoline ligands and copper (II) triflate] using a novel tagging technique for the labeling and identification of members of combinatorial libraries. Chloroarom. diazoketones II (n = 1, 7, 14; R = H, Cl) were used as tagging agents to identify the sequence of reactions to which a resin bead had been subjected; treatment of a resin bead with II in the presence of dirhodium tetrakis(triphenylacetate) yielded a polystyrene resin containing a fraction of chloroaralkyl cycloheptatriene moieties (formed by ring expansion of the polystyrene Ph groups). Oxidative cleavage of the tags with ceric ammonium nitrate liberated the chloroarom. portion of the tags; treatment of the tags with N,O-bis(trimethylsilyl)acetamide and gas chromatog. yielded masses corresponding to the sequence of reactions to which beads were subjected and thus their identities. The tags could be decoded either directly from a bead before compound cleavage, from a bead after compound cleavage, or from compound stock solns. (generated by compound
cleavage
and dissoln. of a fraction of the liberated compds. in THF/H2O). Decoding compound stock solns. was the most effective method of identifying library members; compds. were identified by tag cleavage of solns. containing 1 or 5% of the compound cleaved from a single bead. Stock solns. were decoded most effectively because a fraction of the library member on a given bead was tagged with the chloroarom. diazoketone in addition to the polystyrene resin (due to the high-loading resin used) and because oxidative cleavage of the tags with CAN proceeded more readily in solution than on solid support. A sublibrary of 108 beads chosen from the larger combinatorial library was decoded by this procedure; of the 108 compds., 107 were successfully decoded. Four different synthetic pathways were found to be compatible with the diazoketone tagging methodol. (no data). The use of stock solns. for the decoding and deconvolution of combinatorial libraries is amenable